

Retrospective Analysis of N75-P100 Amplitudes and P100 Latencies of VEPs in Patients Having One-Sided Visual Problems

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Abstract

Background: VEPs of patients who had unilateral visual problems were retrospectively analyzed. The patients N75-P100 amplitudes and P100 latencies of the affected and normal fellow eye were compared. An alternative way of percentage change in amplitude and latency was also correlated with existing (amplitude ratio and absolute prolongation of latency) ways of analysis.

Method: 66 subjects (52 males & 14 Females) selected for study who had either affected left or right eye. Further, mean of N75-P100 amplitudes & mean P100 latencies were compared in affected and normal eye. On the basis of percentage reduction in the N75-P100 amplitude and percentage increase in the P100 latency on affected eye subjects were categorized in to those only with reduced amplitude (Group A), only with increased latency (Group B) or with both reduced amplitude & increased latency (Group C).

Results: Out of 66 patients (mean age 39.50±19.06 yr), 52 were males (78.79%, mean age 38.04±19.22 yr) & 14 were females (21.21%, mean age 44.93±18.11 yr). The patients had nearly equal frequency of affection in right and left eye, with slight preponderance to left eye (LE- n= 38, 57.58%; RE – n= 28, 42.42%). The amplitude reduction (p<0.0001) and latency (p<0.0001) prolongation were significant in affected eye. Group A had maximum number of subjects (n=35; 53.03%) followed by Group C (n=21; 31.82%). We observed a significant inverse correlation (Pearson r = -1.00, p<0.0001) between amplitude ratio & percentage change method and a significant direct correlation (Pearson r = 0.98, p<0.0001) between latency increase and percentage increase of latency.

Conclusion: Frequency of unilateral involvement in both the eyes is nearly equal. Reduction of N75-P100 amplitude is the most commonly observed abnormal VEP parameter. Percentage Change method can be utilized in future for such studies.

Keywords – Visual Evoked Potential (VEP); N75-P100 Amplitude; P 100 Latency; amplitude ratio; latency prolongation; percentage change.

Introduction

Visual evoked potentials (VEPs) depicts electrical phenomena occurring during the visual processing and are a graphic illustration of the cerebral electrical potentials generated by the occipital cortex evoked

by a defined visual stimulus¹. VEP is considered as a procedure of diagnostic and prognostic importance in ophthalmology².

VEP wave components are designated according to their apparent polarity and peak latency. Negative and positive polarities are designated N and P, respectively. Peak latencies are expressed in milliseconds after stimulus. Peaks N75, P100, and N145 are recorded over the occiput after 75, 100 and 145 ms respectively³. N75–P100 amplitude is measured from positive peak of P100 wave to negative peak of preceding N75 wave. The P100

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latency is time of onset of P100 peak after stimulus.

P100 amplitude is considered as the most consistent and reliable wave therefore N75-P100 amplitude and P100 latency can be used as the best parameter for evaluating VEP^{3,4}.

VEP provides a sensitive indication of abnormal conduction in the visual pathway^{5,6}. Increase in conduction time attributed to demyelination can be detected by measuring the P100 latency. Abnormalities in the amplitude of VEP are caused by axonal lesion in the pathway. Hence VEPs are widely used in investigating demyelinating diseases, optic neuritis, and other optic neuropathies^{6,7}.

As there are large differences in VEP among individuals, earlier studies involved comparison of the results for two eyes in the same individual rather than using absolute values of amplitude or latency period^{8,9}. Hence, it is difficult to assess visual function with VEP in cases where both eyes have visual pathway disturbance or functional visual loss combined with visual pathway disability⁸. Previous studies have compared the bilateral eye VEP amplitude, in patients having unilateral eye affection, using amplitude reduction or amplitude ratio i.e. affected/normal eye amplitude and VEP latency in terms of absolute prolongation of latency in ms in affected eye compared to normal eye¹⁰⁻¹³.

Hence we designed a study to retrospectively analyze the N75-P100 amplitudes and P100 latencies of VEPs of patients who presented with diverse visual problems in one of their two eyes. We analyzed N75-P100 amplitudes and P100 latencies of the affected eye and also compared them with that of normal fellow eye of the subjects. We further aimed to validate an alternative method of assessing unilateral VEP abnormalities using percentage decrease of amplitude and percentage increase of latency in affected eye compared to normal eye.

Material and Method

This study was conducted at Saksham Imaging Diagnostic Center and G. R. Medical College Gwalior, M.P., India. This study involves cross sectional retrospective analysis of 66 subjects having unilateral visual problems. The patients either with bilateral eye affection or with bilateral normal VEP were excluded from the study. The patients below 10 yr of age were also excluded as VEP is variable and under maturation

at this stage¹⁴.

The selected patient's data and VEP findings were retrieved. VEPs of normal eye functioned as each subject's internal control. We calculated an N75-P100 amplitude ratio of the affected/normal side for all individuals¹⁰.

Patients were further divided, in to affected left eye or affected right eye on the basis of which of their eye is having visual symptoms and abnormal VEP parameter (Table No.1).

Further mean of N75-P100 amplitudes and P100 latencies of affected and normal fellow eye were compared (Table No.2). Percentage change in amplitude and latency were calculated as follows.

$$\% \downarrow \text{ in Amplitude}^* = (\text{Normal eye Amplitude}^* - \text{Affected eye Amplitude}^*) \times 100$$

$$\text{Normal eye Amplitude}^*$$

$$\% \uparrow \text{ in latency}^\# = (\text{Affected eye Latency}^\# - \text{Normal eye Latency}^\#) \times 100$$

$$\text{Normal eye Latency}^\#$$

Where-

$$^* \text{Amplitude} = \text{N75-P100 amplitude and } ^\# \text{Latency} = \text{P100 latency}$$

Subjects having amplitude ratio <0.80 in affected eye or having >10 ms increase in P100 latency in the affected eye were considered abnormal. Subjects were categorized in to those only with reduced N75-P100 amplitude (Group A), those only with increased P100 latency (Group B) and those with both reduced amplitude & increased latency (Group C)(Table No.3 and Figure No.1).

Correlation analysis between subject's amplitude ratio & percentage change in amplitude and increase in latency & percentage change in latency was done to validate this method for future studies (Figure No.2&3).

Bilateral eye comparisons were done using paired t test. $p < 0.05$ was considered statistically significant. Spearman Pearson analysis was used for correlation. All statistical analysis was done using Graphpad Prism 5.01 software for Windows (Graph-Pad Software, Inc., USA).

Results

VEPs of 66 patients, who had unilateral eye visual affection, were analyzed retrospectively. The mean age of the patients was 39.50 ± 19.06 yr. The number of male patients (78.79%, $n=52$; mean age 38.04 ± 19.22 yr) was higher than the female patients (21.21%, $n=14$; mean age 44.93 ± 18.11 yr).

The patients had nearly equal frequency of affection in right and left eye, with slight preponderance to left eye (LE- $n=38$, 57.58%; RE – $n=28$, 42.42%) (Table No.1).

On affected side the N75-P100 amplitude was significantly reduced ($p < 0.0001$) and P100 latency was significantly ($p < 0.0001$) increased (Table no.2).

Of the total 66 subjects, 56 subjects had reduced N75-P100 amplitude and 31 subjects had prolonged P 100 latency, where 21 subjects had both reduced amplitude and prolonged latency. Hence 35 (53.03 %) subjects had only reduced N75-P100 amplitude (Group A), 10 (15.15%) subjects had only prolonged P100 latency (Group B) and 21 (31.82 %) subjects had both reduced amplitude & prolonged latency (Group C) (Table No.3 and Figure No.1).

43.78 ± 31.11 % decrease in N75-P100 amplitude (amplitude ratio - 0.5638 ± 0.3082) and 12.52 ± 21.98 % increase in latency (prolongation of 9.397 ± 17.65 ms) were observed in affected eye of all subjects. Approximately 50 % decrease in amplitude was observed in Group A (55.26 ± 23.88 % decrease) and Group C (49.09 ± 20.95 % decrease), whereas nearly 30 % increase in latency

was observed in Group B (33.77 ± 20.49 % increase) and Group C (27.79 ± 18.68 % increase) (Table No.3).

There was a significant inverse correlation (Pearson $r = -1.00$, $p < 0.0001$) between amplitude ratio and percentage change method (Figure no.2). Further, we also observed a significant direct correlation (Pearson $r = 0.98$, $p < 0.0001$) between latency increase in the affected eye and percentage increase of latency in the affected eye (Figure no.3).

Table No.1 – Patients grouping on the basis of their affected eye having abnormal VEP parameters

Affected Eye	Males	Females	Total (% of Total)
Right Eye	22	6	28 (42.42%)
Left Eye	30	8	38 (57.58%)
Total	52 (78.79 %)	14 (21.21 %)	66

Table No.2 – Comparison of VEP parameters in affected eye and Normal eye of all the subjects

VEP parameter	Affected eye (n=66)	Normal Eye (n=66)	Level of significance
N75-P100 Amplitude (μ V)	2.294 ± 1.39	4.36 ± 1.98	< 0.0001
P 100 Latency (ms)	104.7 ± 14.69	95.33 ± 17.13	< 0.0001

Table No.3 – Table shows comparative values of VEP parameters in all patients and different groups

Groups	Subjects Showing Change of Parameters in affected eye compared to normal Fellow eye (Number of subjects; % of Total)	Affected/normal eye N75-P100 Amplitude ratio (mean \pm SD)	% Decrease in Amplitude Compared to Fellow eye (mean \pm SD)	Affected - Normal Eye P100 Latency Difference in ms (mean \pm SD)	% Increase in in Latency compared to fellow eye (mean \pm SD)
All subjects	All Subjects ($n=66$; 100%)	0.5638 ± 0.3082	43.78 ± 31.11	9.397 ± 17.65	12.52 ± 21.98
Group A	Subjects Showing Reduced N75-P100 Amplitude ($n=35$; 53.03%)	0.4503 ± 0.2332	55.26 ± 23.88	-3.701 ± 10.89	-2.70 ± 9.59
Group B	Subjects Showing Prolonged P100 Latency ($n=10$; 15.15 %)	1.076 ± 0.1874	-7.55 ± 18.74	28.13 ± 14.03	33.77 ± 20.49
Group C	Subjects showing change in Both Amplitude and Latency ($n=21$; 31.82 %)	0.5091 ± 0.2095	49.09 ± 20.95	21.6 ± 11.43	27.79 ± 18.68

Discussion

This study retrospectively analyzed the data of 66 patients with unilateral eye various visual problems where 132 VEP recordings (66 eyes with normal VEP and 66 eyes with abnormal VEP) were analyzed.

The male subjects were more than the female participants. Some eye conditions have been found to be more prevalent in males¹⁵, where other reports the females more commonly affected with blindness^{16,17}. As this was retrospective analysis of patients referred for VEP, hence this study may not reflect the actual population demographics.

We observed little higher frequency of affection of left eye. There are no any subtle reasons to presume that any one eye is more affected with visual problems than the other^{18,19}. This may be an incidental finding due to small sample size.

Previous studies have compared the bilateral eye amplitudes in patients with one affected eye using the amplitude ratio and absolute increase in latency. They obtained amplitude ratio of affected eye by dividing the affected eye amplitude with normal eye amplitude. Further, they compared the bilateral eye latencies in terms of absolute difference of time in ms (10). We utilized the same method and also used an alternative way of comparison in terms of percentage change as mentioned above. This way has not been used in earlier studies reflecting that it is not a reliable way of comparison. Hence, we correlated percentage change method with the previous method and found a promising correlation between the two methods indicating that this method can also be utilized in future for such studies, where comparison is to be done with one normal eye.

N75-P100 amplitude was reduced in more number of the subjects compared to the number of subjects with prolonged latency. The N75-P100 amplitudes are considered the marker of axonal integrity of optic nerve and P100 latencies are considered to be related to demyelination of optic nerve^{20,21}. Thus more number of subjects were having axonal lesion of optic nerve as the cause of their reduced vision. Optic neuropathy involving axonal lesion have been previously documented as the most common cause of blindness²².

Subjects were grouped on the basis of decrease of amplitudes and increase of P100 latencies in the affected

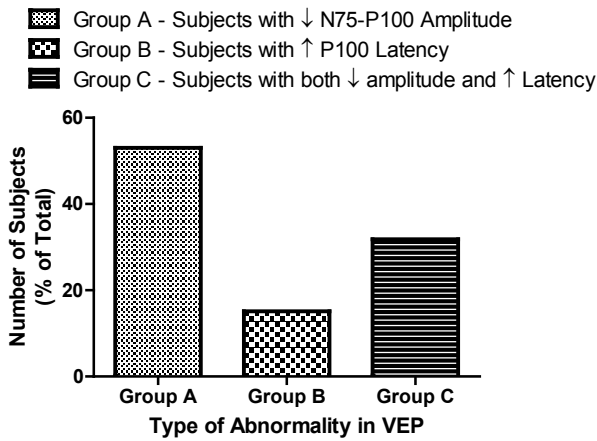


Figure No.1 – Figure shows proportion of subjects in each group based on percentage of Total number of subjects

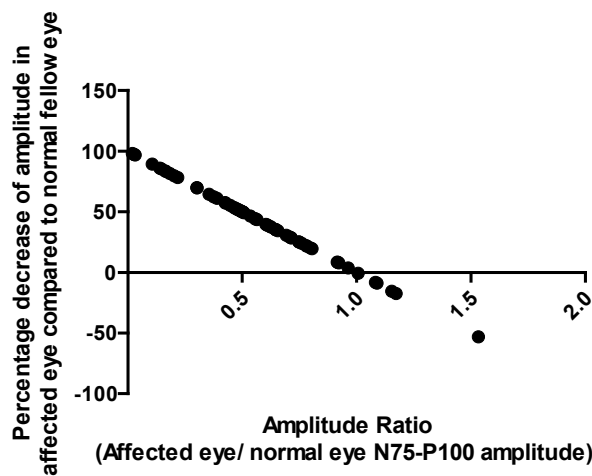


Figure No.2 – Correlation of previously used amplitude ratio method with percentage decrease in N75-P100 amplitude; n=66 (Pearson $r = -1.00$, $p < 0.0001$)

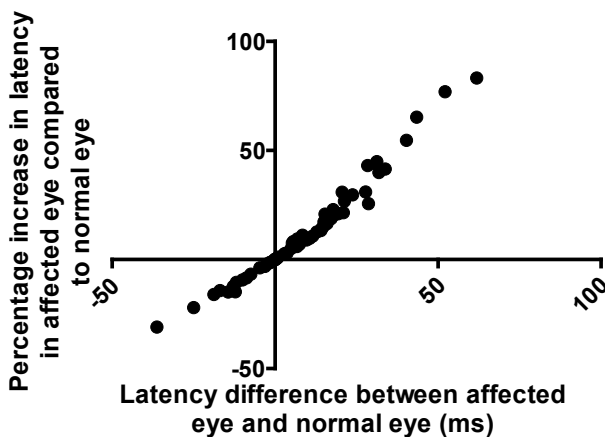


Figure No.3 – Correlation of previously used affected eye and normal eye latency difference method with percentage increase of latency in affected eye; n=66 (Pearson $r = 0.98$, $p < 0.0001$)

eye compared to normal fellow eye in to three groups; Group A only with reduction of N75-P100 amplitude, Group B only with prolongation of P100 latency and Group C having both reduction of amplitude and prolongation of latency. Maximum numbers of subjects were in the Group A followed by Group C. Group B had the least number of subjects. This suggests that there is possibility of all kinds of lesion in reduction of vision. Further, maximum numbers of cases were due to pathologies causing axonal lesion. Moreover, pathologies which lead to both decrease in amplitude and increase in latency were the next common cause of visual loss and least numbers of cases were due to pure demyelinating causes.

Literature have evidences that there are pathological conditions which decrease amplitude or increase latency or do both i.e. decrease amplitude and increase latency together^{10,23-25}. Our study shows the relative frequency of pathological etiologies of axonal, demyelinating and combined axonal and demyelinating lesions in the unilateral visual problems.

Conclusion

Reduction of N75-P100 amplitude is the most commonly observed abnormal VEP parameter suggesting that maximum number of subjects have axonal lesion of optic nerve as the cause of their reduced vision. Percentage change method is also a valid way of comparing the VEP parameters in bilateral eyes if one of the tow eyes has normal VEP.

Funding: NA

Conflict of Interest: There is no conflict of Interest

Ethical approval: Study is approved by institutional Ethics Committee.

References

1. Kothari R, Bokariya P, Singh S, Singh R. A Comprehensive Review on Methodologies Employed for Visual Evoked Potentials. *Scientifica*. 2016; 2016:1-9.
2. Weinstein GW. Clinical aspects of the visually evoked potential. *Trans Am Ophthalmol Soc*. 1977 ;75:627-73.
3. American Clinical Neurophysiology Society. Guideline 9B: guidelines on visual evoked potentials. *Am J Electroneurodiagnostic Technol*. 2006 Sep;46(3):254-74.
4. Kim MK, Kim US. The parameters of pattern visual evoked potential in the severe visual loss patients in Korean. *Korean J Ophthalmol*. 2015 Jun;29(3):185-9.
5. Odom JV, Bach M, Barber C, Brigell M, Marmor MF, Tormene AP, et al. Visual evoked potentials standard (2004). *Documenta Ophthalmologica*. 2004 Mar; 108(2):115-23.
6. Walsh P, Kane N, Butler S. The clinical role of evoked potentials. *Journal of Neurology, Neurosurgery & Psychiatry*. 2005 Jun 1; 76(suppl 2):ii16-22.
7. You Y, Klistorner A, Thie J, Graham SL. Latency delay of visual evoked potential is a real measurement of demyelination in a rat model of optic neuritis. *Invest Ophthalmol Vis Sci*. 2011 Aug 29;52(9):6911-8.
8. Jeon J, Oh S, Kyung S. Assessment of visual disability using visual evoked potentials. *BMC Ophthalmol*. 2012 Aug 6; 12:36.
9. Sokol S. Pattern visual evoked potentials: their use in pediatric ophthalmology. *Int Ophthalmol Clin*. 1980; 20(1):251-68.
10. Holmes MD, Sires BS. Flash visual evoked potentials predict visual outcome in traumatic optic neuropathy. *Ophthalmic Plast Reconstr Surg*. 2004 Sep;20(5):342-6.
11. Alshowaeir D, Yiannikas C, Fraser C, Klistorner A. Mechanism of delayed conduction of fellow eyes in patients with optic neuritis. *Int J Ophthalmol*. 2018;11(2):329-32.
12. Gündüz K, ZengİN N, Okudan S, Okka M, Özbayrak Ni. Pattern-reversal electroretinograms and visual evoked potentials in branch retinal vein occlusion. *Doc Ophthalmol*. 1995 Jun 1;91(2):155-64.
13. Andrade EP, Berezovsky A, Sacai PY, Pereira JM, Rocha DM, Salomão SR, et al. Dysfunction in the fellow eyes of strabismic and anisometropic amblyopic children assessed by visually evoked potentials. *Arquivos Brasileiros de Oftalmologia*. 2016 Oct;79(5):294-8.
14. Yadav R, Hari Poudel B, Limbu N, Thakur D, Kumar Yadav S. Normative data of Visual Evoked

- Potential in children and correlation with age. Asian Journal of Medical Sciences. 2015 Nov 5;7:39.
15. Akhtar F, Micheal S, Khan M, S Y, M B, Ahmed A, et al. Does gender have an effect in the Prevalence of types of glaucoma in Pakistani population? Al-Shifa Journal of Ophthalmology. 2010 Jan 1;6:30–6.
 16. Courtright P, Bassett K. Gender and Blindness: Eye Disease and the Use of Eye Care Services. Community Eye Health. 2003; 16(45):11–2.
 17. Khandekar R, Mohammed AJ. Gender inequality in vision loss and eye diseases: Evidence from the Sultanate of Oman. Indian J Ophthalmol. 2009 ;57(6):443–9.
 18. Buch H, Vinding T, La Cour M, Nielsen NV. The prevalence and causes of bilateral and unilateral blindness in an elderly urban Danish population. The Copenhagen City Eye Study. Acta Ophthalmol Scand. 2001 Oct;79(5):441–9.
 19. Bajracharya K, Gautam P, Yadav SK, Shrestha N. EPIDEMIOLOGY AND CAUSES OF OPTIC ATROPHY IN GENERAL OUTPATIENT DEPARTMENT OF LUMBINI EYE INSTITUTE. :4.
 20. Walsh P, Kane N, Butler S. The clinical role of evoked potentials. Journal of Neurology, Neurosurgery & Psychiatry. 2005 Jun 1;76(suppl 2):ii16–22.
 21. Diem R, Tschirne A, Bähr M. Decreased amplitudes in multiple sclerosis patients with normal visual acuity: A VEP study. Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia. 2003 Feb 1;10:67–70.
 22. Ghaffarieh A, Levin LA. Chapter One - Optic Nerve Disease and Axon Pathophysiology. In: Goldberg JL, Trakhtenberg EF, editors. International Review of Neurobiology. Academic Press; 2012. p. 1–17. (Axon Growth and Regeneration: Part 1; vol. 105).
 23. Samsen P, Chuenkongkaew WL, Masayaanon P, Chirapapaisan N, Ruangvaravate N, Loket S. A comparative study of visual evoked potentials in optic neuritis and optic neuritis with multiple sclerosis. J Med Assoc Thai. 2007 Feb;90(2):313–8.
 24. Papathanasopoulos PG, Papakostopoulos D. Pattern reversal visual evoked potentials in retinitis pigmentosa. International Journal of Psychophysiology. 1994 May 1;16(2):245–50.
 25. Alshuaib WB. Progression of visual evoked potential abnormalities in multiple sclerosis and optic neuritis. Electromyogr Clin Neurophysiol. 2000 Jun;40(4):243–52.